5-ARYLTETRAZOLE COMPOUNDS, COMPOSITIONS THEREOF, AND USES THEREFOR

This application is a continuation-in-part of U.S. application no. 10/197,609, filed July 18, 2002, which is currently pending, the entirety of which is incorporated herein by reference.

GOVERNMENTAL SUPPORT

The research leading to the invention was supported, at least in part, by a grant from: the National Institute of General Medical Sciences Grant No. 1R43 GM63274-01A1; the National Heart, Lung, and Blood Institute Grant No. 1R43HL70342-01; the National Institute of General Medical Sciences Grant No. 2R44GM59017-02; and the National Institute of General Medical Sciences Grant No. 1R43GM59017-01. Accordingly, the U.S. Government may have certain rights in the invention.

1. FIELD OF THE INVENTION

The present invention relates to 5-Aryltetrazole Compounds, compositions comprising an effective amount of a 5-Aryltetrazole Compound, and methods for treating or preventing an inflammation disease, a reperfusion disease, or hyperuricemia comprising administering to an animal in need thereof an effective amount of a 5-Aryltetrazole Compound.

2. BACKGROUND OF THE INVENTION

The level of xanthine oxidase ("XO") in an animal increases markedly (>400-fold in bronchoalveolar fluid in pneumonitis) during inflammation, ischemia-reperfusion injury, and atherosclerosis. Particularly, due to the spillover of tissue XO into the circulation, plasma levels of XO may be detected in an animal experiencing adult respiratory distress syndrome, ischemia-reperfusion injury, arthritis, sepsis, hemorrhagic shock, and other inflammatory conditions. Inflammation-induced histamine release by mast cells and basophils also enhances the activity of XO.

Superoxide radical (O_2^-) can be generated by xanthine oxidase and NADPH oxidase from the partial reduction of molecular oxygen. Neutrophils and macrophages are known to produce O_2^- and hydrogen peroxide (H_2O_2), which normally are involved in the killing of ingested or invading microbes (T. Oda *et al.*, *Science*, 244:974-976). Under physiologic conditions XO is ubiquitously present in the form of a xanthine dehydrogenase (XDH). XDH is a molybdenum iron-sulfur flavin dehydrogenase that uses NAD^+ as an